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## **Endovascular cooling with heat exchange catheters: a new method to induce and maintain hypothermia**

Keller, Emanuela ; Imhof, Hans-Georg ; Gasser, Stefan ; Terzic, Andre ; Yonekawa, Yasuhiro

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## **Endovascular cooling with heat exchange catheters: a new method to induce and maintain hypothermia**

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## Abstract

*Objective:* To test the convenience of a new cooling technique with intravenous heat exchange catheters. *Design:* Retrospective chart review. *Setting:* University hospital neurointensive care unit. *Patients:* 20 patients with severe subarachnoid hemorrhage Hunt and Hess Grade 3 – 5 treated with mild hypothermia. *Interventions:* In all patients cooling to reach target body core temperature (33°C–34°C) was induced as quickly as possible. In the first 10 patients (group one) moderate hypothermia was induced and maintained using cooling blankets. In group two a 8.5F heat exchange catheter was placed central venous and temperature-adjusted normal saline circulated in a closed-loop system entailing two balloons. *Measurements and results:* A total of 2007 values of body core temperature (BCT) were registered every hour. Foley temperature catheters were used for monitoring BCT in the bladder. The time to reach the target BCT and the stability of temperature during hypothermia were compared between the two groups. No specific complications associated with the new cooling device were observed. Time to reach the target temperature in group two was significantly shorter than in group one ( $190 \pm 110$  and  $370 \pm 220$  mins) ( $p=0.023$ ). In group one significantly more temperature values were out of the target range (127 of 792 values;16.0%) than in group two (62 of 1215 values;5.1%) ( $p<0.0001$ ). *Conclusions:* The new endovascular cooling technique seems to be superior for rapid induction of hypothermia and maintaining temperature more stable than the cooling techniques using blankets and ice bags.

## Key words

Hypothermia; endovascular cooling, heat exchange catheter, subarachnoid hemorrhage

## **Introduction**

Animal and clinical studies show that hypothermia has the potential to limit the extent of secondary brain damage (1-11). Rapid cooling measures, stability of temperature during treatment and controlled rewarming are essential for optimal use of hypothermia. Currently, hypothermia is being induced by surface cooling using cooling blankets, skin washing with alcohol and ice bags. In a preliminary report in six patients with hemispheric infarction Georgiadis et al. suggest that induction and maintenance of hypothermia with a new intravenous cooling device are feasible (12) Nevertheless, to date no comparative studies with conventional cooling techniques were performed.

The aim of the present study was to test the convenience and to examine possible advantages of the new cooling technique with intravenous heat exchange catheters.

## **Materials and methods**

From September 1999 to September 2001 20 patients (7 men and 13 woman) with subarachnoid hemorrhage (SAH) Hunt and Hess Grade 3 to 5 were treated with moderate hypothermia. The protocol was part of a project approved by the Ethics Committee of the University of Zürich (E-015/99). Informed consent was obtained by the next of kin or legal representatives.

All patients were sedated (fentanyl infusion 5 - 8 ug/kg/h and midazolam 0.1 – 0.4 mg/kg/h) and received neuromuscular blockade (atracurium 0.3 to 0.6 mg/kg/h). The patients were ventilated with a volume-controlled, pressure-regulated mode (EVITA

4, Dräger, Lübeck, Germany). Mean arterial pressure (MAP), cardiac output (CO), intrathoracic blood volume (ITBV) and extravascular lung water (EVLW) were monitored by a thermodilution catheter inserted in the femoral artery (PICCO system, Pulsion, Munich, Germany). Intracranial pressure (ICP) was monitored using ventricular catheters or subdural probes (NMT Neuroscience, Frankfurt, Germany) or intraparenchymatous sensors and transducers (Codman microsensor, Johnson & Johnson, Raynham). Body core temperature (BCT) values were registered every hour. Foley temperature catheters (temperature resolution 0.1°C) were used for monitoring BCT in the bladder (Mon-a-therm, Mallinckrodt, Hazelwood, MO, USA). Room temperature in the intensive care unit was between 20°C and 22°C.

If ICP increased above 15mmHg after early aneurysm surgery (day 0-1) patients were treated with drainage of cerebrospinal fluid, osmotherapy (Mannitol 20% and hypertonic NaCl-hydroxyethyl-starch solution), mild hyperventilation and tris-hydroxymethyl-aminomethane (THAM) buffer. If these conventional methods failed to control elevated ICP, the patients were first treated with barbiturate coma. Barbiturate coma was induced with a thiopental loading dose of 10mg/kgBW, followed by a continuous infusion according to burst suppression pattern in continuous EEG. Nevertheless, instead of above listed treatment, if ICP continued to increase >15mmHg cooling to reach the target BCT of 33°C to 34°C was induced as quickly as possible. If ICP further increased > 15 mmHg a decompressive craniectomy with external decompression (removal of a large bone flap with dural patch with polyesterurethane/collagen) was performed. The target values for blood pressure management were adapted to reach cerebral perfusion pressure (CPP) values above 70 mmHg. All patients were treated under extended monitoring of cerebral hemodynamics (monitoring of jugular bulb O<sub>2</sub>-saturation, cerebral blood flow or intraparenchymatous O<sub>2</sub> partial pressure) (13,14). Hypothermia combined with

barbiturate coma was maintained depending on the course of ICP. Patients rewarming was initiated not before ICP remained stable  $<15$  mmHg for more than 24 hours. If CT control confirmed decrease of signs of brain edema patients were rewarmed no faster than  $1^{\circ}\text{C}$  per 24 hours. Normothermia thereafter was reached within two to three days.

Between September 1999 and September 2000 in 10 patients (group one) moderate hypothermia was induced and maintained by surface cooling using cooling blankets (Bair Hugger<sup>TM</sup>, Augustine Medical, Saint Prarie; MN, USA and Blanketrol, CSZ, Cincinnati; OH, USA) and ice bags on groin, axilla and neck. Between October 2000 and October 2001 in group two a dual infusion lumen 8.5F 20 cm catheter was placed central venous via the subclavian vein into the superior vena cava or via the femoral vein into the vena illiaca (Cool Line Catheter, Alsius Corporation, Irvine, CA, USA). The catheter is furnished with an additional lumen, which ends in two balloons, sized 55 in lengths and 5x5 mm in diameter. The balloons are perfused with a sterile Ringerlactate solution via a closed-loop tubing system. The tubing system is connected to a temperature-management device (Coolgard System, Alsius Corporation, Irvine, CA, USA), consisting of a temperature adjustable water bath ( $0.5^{\circ}\text{C}$  to  $42^{\circ}\text{C}$ ) depending on the patient's own temperature. A pump circulates the Ringerlactate solution through the water bath.

The following side effects of hypothermia were recorded: Pneumonia was defined as new infiltrates on chest x-ray combined with purulent tracheobronchial secretion. Sepsis was defined as systemic inflammatory response with underlying infection (15). Bradycardia ( $<40$  beats per minute) and cardiac arrhythmias were documented. Signs of hemolysis were indicated by an increase of lactate dehydrogenase above two-fold values and confirmed by an increase of direct bilirubine in serum.

Complications of hypothermia, time to reach the target BCT, stability of temperature during hypothermia and Glasgow Outcome Score (GOS) were compared between the two groups. The time to reach the target BCT was calculated from the beginning of the Cool Line catheter installation until BCT target temperature  $\leq 34^{\circ}\text{C}$  was reached. Neurological outcome was assessed after three months in the outpatient clinic by a neurologist, who was blinded to the management of the patients during their ICU stay, using the Glasgow Outcome Score (GOS) (16), where GOS 1 denominates death, GOS 2 vegetative state (unable to interact with the environment), GOS 3 severe disability (unable to live independently but able to follow commands), GOS 4 moderate disability (capable of living independently but unable to return to work or school) and GOS 5 mild or no disability (able to return to work or school). Those patients who did not show up on control were contacted and asked about their functional status.

### Statistical analysis

To compare the two groups the Mann-Whitney test was used; to compare the BCT values out of target range the Chi-square test was used. Statistical significance was assumed at a p-value  $<0.05$ .

## Results

There were no differences concerning age, severity of SAH, duration of hypothermia and BCT before induction of hypothermia between the two patient groups (table 1).

No specific complications associated using the new cooling device were observed.

The catheters were carefully inspected upon removal. The balloons of all catheters

were intact and no thrombus formation was macroscopically visible. No signs of hemolysis, no relevant hematomas and no episode of severe bradycardia occurred. Possible complications of hypothermia are given in table 2. All 20 patients developed severe infections. Pneumonia occurred in 16 patients, one patient developed craniotomy wound infection and one patient with mycotic aneurysm developed endocarditis. Four patients developed sepsis syndrome. One patient in group two with coronary artery disease and preexisting hypertensive renal disease developed supraventricular tachycardia, successfully treated with amiodarone. Three patients, all in group one, died from severe ARDS (acute respiratory distress syndrome). Thrombocytopenia ( $< 100\ 000$  platelets per cubic millimeter) occurred in seven patients. Serum levels of amylase were elevated ( $>53$  U/L) in all patients but without other clinical or sonographic signs of pancreatitis. GOS in all patients, group one and two are given in table 3. Median GOS in all patients was 4. In group one GOS<sub>median</sub> was 2.5 and in group two 4.5. In all patients showing signs of systemic inflammatory response intravenous and intraarterial catheters were changed. In group two Cool Line catheters were not more often colonized with microorganisms (two from 16 catheters; 12.5%) than other intravenous catheters (subclavian and jugular bulb catheters) (six from 34 catheters; 17.6%).

In the 20 patients a total of 2007 values of body core temperature (BCT) were registered every hour (table 4). The mean duration of hypothermia in all patients was  $100 \pm 83$  hours (range, 8 to 354 hours). The time needed for Cool Line catheter insertion ranged from 10 to 25 minutes. Mean time to reach the target temperature in group two was significantly shorter than in group one ( $190 \pm 110$  and  $370 \pm 220$  mins) ( $p=0.023$ ). In group one significantly more temperature values were out of the target range (127 of 792 values; 16.0%) than in group two (62 of 1215 values; 5.1%) ( $p<0.001$ ) (figure 1).



## Discussion

Animal and clinical studies showed that moderate hypothermia has neuroprotective properties in severe traumatic brain injury, subarachnoid hemorrhage (SAH), and ischemia (3-7,9-11,17,18). Preliminary clinical studies suggest that moderate hypothermia may improve outcome in patients with malignant middle cerebral artery infarction and after cardiac arrest (8, 10, 11, 19). Nevertheless, in 50 patients with hemispheric infarction treated with moderate hypothermia 15 patients died during or after rewarming because of excessive ICP rise (8). The authors found that a shorter (<16 hours) rewarming period was associated with more pronounced increases in ICP and concluded that a longer period of controlled rewarming may limit death caused by rebound edema. It is to be assumed that not only controlled rewarming but stability of temperature during treatment are most important for optimal use of hypothermia. With the new cooling technique less temperature values were out of the target range during maintenance of hypothermia.

Furthermore, animal experiments indicate that hypothermia should be induced as early as possible in the course of illness (2,3,17,20-23). Moreover, in case of obese patients reaching the target BCT within time by surface cooling might be difficult (18). Therefore rapid and effective cooling measures are needed for induction of hypothermia. In the group with endovascular cooling time to insert the Cool Line catheter and to reach target BCT was in mean three hours, which was significantly shorter than in the group treated with conventional cooling techniques. Our results are comparable to the preliminary observations in six patients with hemispheric infarction made by Georgiadis et al. who reached the required target temperature in  $3 \pm 1$  hours (without catheter installation) (12).

BCT temperature was estimated from a thermistor catheter in the urinary bladder. Blood temperature as the standard for the BCT was monitored by a thermodilution catheter inserted in the femoral artery. Nevertheless, in group one these values were often influenced by ice bags on groin. Urinary bladder temperature monitoring has been shown to correlate well with the pulmonary arterial blood temperature (24).

With the new endovascular cooling device no specific complications associated with the technique occurred. No signs of hemolysis and no relevant hematomas from puncture sites occurred. Thrombocytopenia and colonization with microorganisms did not appear more often when using the heat exchange catheters.

Glasgow Outcome Score in the endovascular cooling group seems to be better than in the group treated with cooling blankets. Nevertheless, one might not conclude that the application of the new endovascular cooling device independently improves the outcome in patients treated with hypothermia after SAH. In the present study uncontrolled patient groups in consecutive time periods are compared retrospectively. Having become more experienced in hypothermia treatment over the two years period, other factors in neurointensive care management might have changed and influenced the outcome as well.

In conclusion, the new endovascular cooling technique seems to be superior for rapid induction of hypothermia and maintaining temperature more stable than the cooling techniques using blankets and ice bags. It is to be assumed that during slow rewarming BCT is easier to control with the new device than with conventional techniques. To show the safety of the new technique and to examine whether the new method improves the outcome of patients treated with hypothermia, examinations in a larger set of ICU patients are needed.

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## Figure legends

### Figure 1: Stability of temperature

In group one significantly more temperature values were out of the target range of 33-34°C (127 of 792 values;16.0%) than in group two (62 of 1215 values;5.1%).

Scattergram and box and whiskers extending from the 25th to the 75th percentile show that BCT during hypothermia is more stable in group two.

BCT, body core temperature